Proprietary Preparations (details are given in Part 3)
Arg.: Fioritina; ***Austral.:*** Levophed; ***Belg.:*** Levophed; Norepine†; ***Braz.:*** Levophed; Norephed†; ***Canad.:*** Levophed; ***Chile:*** Adine; ***Ger.:*** Arterenol; ***Gr.:*** Levophed; Noradren; ***Hong Kong:*** Levophed†; ***India:*** Adrenor; ***Indon.:*** Levophed; N-Epi; Raivas; Vascon; ***Irl.:*** Levophed; ***Israel:*** Levophed; ***Malaysia:*** Levophed; ***Mex.:*** Pridam; ***NZ:*** Levophed; ***Philipp.:*** Inotrop; Levophed; ***Pol.:*** Levonor; ***Singapore:*** Levophed†; ***Spain:*** Norages; ***Thai.:*** Levophed; ***USA:*** Levophed.

Used as an adjunct in: ***Austria:*** Neo-Xylestesin forte; Scandonest; ***Braz.:*** Xylestesin; Xylocaina; ***Ger.:*** Xylestesin-S†; Xylestesin, Xylestesin-F†; ***Ital.:*** Lident Andrenor†; Xylonor; ***Port.:*** Scandonest; Xilonibsa; ***S.Afr.:*** Xylotox; ***Spain:*** Xylonor Especial; ***Switz.:*** Scandonest; Xylestesin-F†; Xylestesin-S "special"†; ***Thai.:*** Neo-Lidocaton†.

Norfenefrine Hydrochloride *(rINNM)* ⊗

Hidrocloruro de norfenefrina; Norfenefrin Hidroklorür; Norfénéfrine, Chlorhydrate de; Norfenefrini Hydrochloridum; Norphenylephrine Hydrochloride; *m*-Norsynephrine Hydrochloride; WV-569. 2-Amino-1-(3-hydroxyphenyl)ethanol hydrochloride.

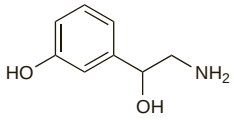
Норфенефрина Гидрохлорид

$C_8H_{11}NO_2,HCl$ = 189.6.

CAS — 536-21-0 (norfenefrine); 15308-34-6 (norfenefrine hydrochloride).

ATC — C01CA05.

ATC Vet — QC01CA05.



(norfenefrine)

NOTE. *m*-Octopamine has been used as a synonym for norfenefrine. Care should be taken to avoid confusion with octopamine, which is the *p*-isomer.

Profile

Norfenefrine is a sympathomimetic (p.1407) with predominantly alpha-adrenergic activity. It is used as the hydrochloride for its vasopressor effect in the treatment of hypotensive states (p.1174). The usual oral dose is 15 mg three times daily of norfenefrine hydrochloride, as a modified-release preparation. Norfenefrine hydrochloride has also been given by injection.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Novadral; ***Ger.:*** Novadral†; ***Mex.:*** AS Cor; ***Switz.:*** Novadral; ***Turk.:*** Novadral.

Multi-ingredient: ***Ger.:*** Adyston†; Normotin-R†; Ordinal Forte†; ***Switz.:*** Ortho-Maren retard.

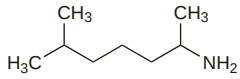
Octodrine *(USAN, rINN)* ⊗

Octodrina; Octodrinum; SKF-51. 1,5-Dimethylhexylamine.

Октодрин

$C_8H_{19}N$ = 129.2.

CAS — 543-82-8.



Profile

Octodrine is a sympathomimetic (p.1407) with mainly alpha-adrenergic activity. It has been given orally as the camsilate, in combination with norfenefrine (p.1361), in the treatment of hypotensive states. Octodrine phosphate has been used as an ingredient of preparations for obstructive airways disease.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austria:*** Ambredin; ***Ger.:*** Ordinal Forte†.

Olmesartan Medoxomil *(BAN, USAN, rINN)*

CS-866; Olmésartan Médoxomil; Olmesartán medoxomilo; Olmesartanum Medoxomilum; RNH-6270 (olmesartan). (5-Methyl-2-oxo-1,3-dioxol-4-yl) methyl ester of 4-(1-Hydroxy-1-methylethyl)-2-propyl-1-{[2′-(1*H*-tetrazol-5-yl)[1,1′-biphenyl]-4-yl]methyl}-1*H*-imidazole-5-carboxylic acid.

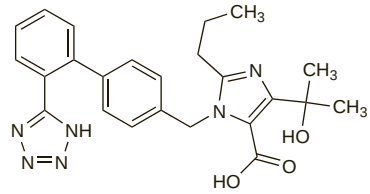
Ольмезартан Медоксомил

$C_{29}H_{30}N_6O_6$ = 558.6.

CAS — 144689-24-7 (olmesartan); 144689-63-4 (olmesartan medoxomil).

ATC — C09CA08.

ATC Vet — QC09CA08.



(olmesartan)

NOTE. The name olmesartan has been applied to both the base and to the medoxomil ester.

Adverse Effects and Precautions

As for Losartan Potassium, p.1326.

Interactions

As for Losartan Potassium, p.1327.

Pharmacokinetics

Olmesartan medoxomil is an ester prodrug that is hydrolysed during absorption from the gastrointestinal tract to the active form olmesartan. The absolute bioavailability is about 26%. Peak plasma concentrations of olmesartan occur about 1 to 2 hours after oral doses. Olmesartan is at least 99% bound to plasma proteins. It is excreted in the urine and the bile as olmesartan; about 35 to 50% of the absorbed dose is excreted in the urine and the remainder in the bile. The terminal elimination half-life is between 10 and 15 hours.

◊ References.

1. Yoshihara K, *et al.* Population pharmacokinetics of olmesartan following oral administration of its prodrug, olmesartan medoxomil: in healthy volunteers and hypertensive patients. *Clin Pharmacokinet* 2005; **44:** 1329–42.

Uses and Administration

Olmesartan is an angiotensin II receptor antagonist with actions similar to those of losartan (p.1327). It is used in the management of hypertension (p.1171).

Olmesartan is given orally as the ester prodrug olmesartan medoxomil. After a dose the hypotensive effect lasts for 24 hours. Most of the hypotensive effect is apparent within 2 weeks after starting therapy and is maximal within about 8 weeks.

In hypertension, olmesartan medoxomil is given in a usual dose of 20 mg once daily, although in the UK an initial dose of 10 mg once daily is recommended. The dose may be increased to 40 mg once daily if required.

For doses in hepatic or renal impairment, see below.

◊ References.

1. Brunner HR. The new oral angiotensin II antagonist olmesartan medoxomil: a concise overview. *J Hum Hypertens* 2002; **16** (suppl 2): S13–S16.
2. Warner GT, Jarvis B. Olmesartan medoxomil. *Drugs* 2002; **62:** 1345–53. Correction. *ibid.*; 1852.
3. Gardner SF, Franks AM. Olmesartan medoxomil: the seventh angiotensin receptor antagonist. *Ann Pharmacother* 2003; **37:** 99–105.
4. Unger T, *et al.* The role of olmesartan medoxomil in the management of hypertension. *Drugs* 2004; **64:** 2731–9.
5. Mire DE, *et al.* A review of the structural and functional features of olmesartan medoxomil, an angiotensin receptor blocker. *J Cardiovasc Pharmacol* 2005; **46:** 585–93.
6. Takai S, Miyazaki M. Effect of olmesartan medoxomil on atherosclerosis: clinical implications of the emerging evidence. *Am J Cardiovasc Drugs* 2006; **6:** 363–6.
7. Smith DH. Dose-response characteristics of olmesartan medoxomil and other angiotensin receptor antagonists. *Am J Cardiovasc Drugs* 2007; **7:** 347–56.
8. Zannad F, Fay R. Blood pressure-lowering efficacy of olmesartan relative to other angiotensin II receptor antagonists: an overview of randomized controlled studies. *Fundam Clin Pharmacol* 2007; **21:** 181–90.
9. Chrysant SG, *et al.* Treatment of hypertension with olmesartan medoxomil, alone and in combination with a diuretic: an update. *J Hum Hypertens* 2007; **21:** 699–708.
10. Barrios V, Escobar C. Olmesartan medoxomil plus hydrochlorothiazide for treating hypertension. *Expert Opin Pharmacother* 2008; **9:** 129–36.

Administration in hepatic or renal impairment. Olmesartan is excreted in both urine and bile and raised plasma concentrations have been noted in patients with renal or hepatic impairment. In patients with *renal impairment*, licensed product information in the UK does not recommend the use of olmesartan in severe impairment (creatinine clearance (CC) below 20 mL/minute) since experience is limited, and the maximum dose in mild to moderate impairment (CC 20 to 60 mL/minute) is 20 mg once daily. Similarly, in patients with *hepatic impairment*, licensed product information in the UK does not recommend the use of olmesartan in severe impairment since there is no experience. Those with moderate hepatic impairment should be given an initial dose of 10 mg once daily and the maximum dose is 20 mg once daily.

Migraine. For reference to the use of angiotensin II receptor antagonists, including olmesartan, in the prophylaxis of migraine, see under Losartan, p.1328.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Olmec; Tensonit; Vasexten; ***Austral.:*** Olmetec; ***Austria:*** Olmetec; ***Belg.:*** Belsar; Olmetec; ***Braz.:*** Benicar; Olmetec; ***Cz.:*** Olmetec; Sarten; ***Denm.:*** Olmetec; ***Fin.:*** Benetor; Olmetec; ***Fr.:*** Alteis; Olmetec; ***Ger.:*** Olmetec; Votum; ***Gr.:*** Olartan; Olmetec; ***Hong Kong:*** Olmetec; ***Indon.:*** Olmetec; ***Irl.:*** Benetor; Omesar; ***Israel:*** Olmetec; ***Ital.:*** Olmetec; Olpress; Plaunac; ***Jpn:*** Olmetec; ***Malaysia:*** Olmetec; ***Neth.:*** Olmes; Olmetec; ***Norw.:*** Olmetec; ***Philipp.:*** Olmetec; ***Port.:*** Olmetec; Olsar; ***Singapore:*** Olmetec; ***Spain:*** Ixia; Olmetec; Openvas; ***Switz.:*** Olmetec; Votum; ***Thai.:*** Olmetec; ***UK:*** Olmetec; ***USA:*** Benicar; ***Venez.:*** Benicar; Olmetec.

Multi-ingredient: ***Austral.:*** Olmetec Plus; ***Belg.:*** Olmetec Plus; ***Braz.:*** Benicar HCT; Olmetec HCT; ***Cz.:*** Olmetec Plus H; Sarten Plus H; ***Fr.:*** Alteisduo; Coolmetec; ***Ger.:*** Olmetec Plus; Votum Plus; ***Gr.:*** Olartan Plus; Olmetec Plus; ***Malaysia:*** Olmetec Plus; ***Port.:*** Olsar Plus; ***Singapore:*** Olmetec Plus; ***Switz.:*** Olmetec Plus; Votum Plus; ***UK:*** Olmetec Plus; ***USA:*** Azor; Benicar HCT.

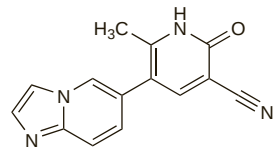
Olprinone Hydrochloride *(rINNM)*

Hidrocloruro de olprinona; Olprinone, Chlorhydrate d'; Olprinoni Hydrochloridum. 1,2-Dihydro-5-imidazo[1,2-*a*]pyridin-6-yl-6-methyl-2-oxonicotinonitrile hydrochloride.

Ольпринона Гидрохлорид

$C_{14}H_{10}N_4O,HCl$ = 286.7.

CAS — 106730-54-5 (olprinone); 119615-63-3 (olprinone hydrochloride).



(olprinone)

Profile

Olprinone is a phosphodiesterase inhibitor with positive inotropic and vasodilator activity, used in acute heart failure (p.1165). It is given intravenously as the hydrochloride in an initial dose of 10 micrograms/kg given over 5 minutes, followed by a continuous infusion at a rate of 100 to 400 nanograms/kg per minute, according to response.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Coretec.

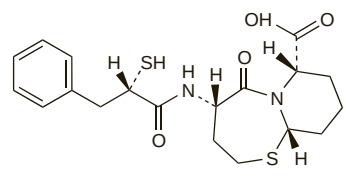
Omapatrilat *(BAN, USAN, rINN)*

BMS-186716; BMS-186716-01; Omapatrilate; Omapatrilato; Omapatrilatum. (4*S*,7*S*,10a*S*)-Octahydro-4-[(*S*)-α-mercaptohydrocinnamamido]-5-oxo-7*H*-pyrido[2,1-*b*][1,3]thiazepine-7-carboxylic acid.

Омапатрилат

$C_{19}H_{24}N_2O_4S_2$ = 408.5.

CAS — 167305-00-2.



Profile

Omapatrilat is a vasopeptidase inhibitor. It inhibits both angiotensin-converting enzyme and neutral endopeptidase and is under investigation in the management of hypertension and heart failure. However, its use may be limited by severe angioedema.

◊ References.

1. Tabrizchi R. Dual ACE and neutral endopeptidase inhibitors: novel therapy for patients with cardiovascular disorders. *Drugs* 2003; **63:** 2185–2202.
2. Kostis JB, *et al.* Omapatrilat and enalapril in patients with hypertension: the Omapatrilat Cardiovascular Treatment vs. Enalapril (OCTAVE) trial. *Am J Hypertens* 2004; **17:** 103–11.

Omega-3 Fatty Acids

Ácidos grasos omega 3.

Омега-3 Жирные Кислоты

ATC — C10AX06.

ATC Vet — QC10AX06.

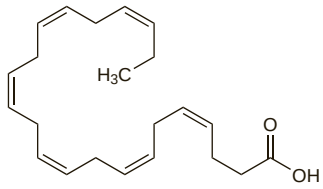
Docosahexaenoic Acid

Doconexent *(rINN)*; Cervonic Acid; DHA; Doconexento; Doconexentum. (*all-Z*)-Docosahexa-4,7,10,13,16,19-enoic acid.

Доконексент

$C_{22}H_{32}O_2$ = 328.5.

CAS — 6217-54-5; 25167-62-8.



NOTE. DHA is also used as a synonym for dihydroxyacetone (p.1594).

Docosahexaenoic Acid Ethyl Ester

Doconexent Ethyl *(rINNM)*; Cervonic Acid Ethyl Ester; Doconexent d'Éthyle; Doconexento de etilo; Ethyl Docosahexaenoate; Ethylum Doconexentum.

Этил Доконексент

$C_{24}H_{36}O_2$ = 356.5.

CAS — 81926-94-5 (all-Z); 84494-72-4.

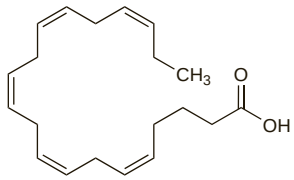
Eicosapentaenoic Acid

Icosapent *(rINN)*; Acidum Eicosapentaenoicum; Eikosapentaeenihappo; Eikosapentaensyra; EPA; Icosapento; Icosapentum; Timnodonic Acid. (*all-Z*)-Eicosapenta-5,8,11,14,17-enoic acid.

Икозапент

$C_{20}H_{30}O_2$ = 302.5.

CAS — 10417-94-4 (all-z); 1553-41-9.



NOTE. EPA is also used as a synonym for pheneturide.

Eicosapentaenoic Acid Ethyl Ester

Icosapent Ethyl *(rINNM)*; Ethyl Eicosapentaenoate; Ethyl Icosapentate; Ethylum Icosapentum; Icosapent d'Ethyle; Icosapento de etilo; Timnodonic Acid Ethyl Ester.

Этил Икозапент

$C_{22}H_{34}O_2$ = 330.5.

CAS — 73310-10-8 (all-Z); 86227-47-6 (all-Z); 84494-70-2.

Pharmacopoeias. In *Jpn.*

Linolenic Acid

ALA; Alpha-linolenic Acid; Kwas linolenowy; α-Linolenic Acid. (*all-Z*)-9,12,15-Octadecatrienoic acid.

Линоленовая Кислота

$C_{18}H_{30}O_2$ = 278.4.

CAS — 463-40-1.

NOTE. Do not confuse with γ-linolenic acid (Gamolenic Acid, p.2308)

Omega-3-acid Ethyl Esters *(USAN)*

Ethylestery omega-3-kyselin; K-85; Omega-3 Acidorum Esteri Ethylici; Omega-3 Acidorum Esteri Ettylici; Omega-3 rūgščių etilo esteriai; Omega-3-sav-etilészterek.

Омега-3-кислоты Этиловых Эфиров

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Omega-3-Acid Ethyl Esters 60). A mixture of ethyl esters of omega-3 acids. They are obtained by transesterification of the body oil of fat fish species coming from families such as Engraulidae, Carangidae, Clupeidae, Osmeridae, Salmonidae, and Scombridae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (timnodonic acid), heneicosapentaenoic acid, clupanodonic acid, and docosahexaenoic acid (cervonic acid). The total amount of omega-3 acid ethyl esters, eicosapentaenoic acid ethyl esters, and docosahexaenoic acid ethyl esters should be stated on the label. For a total omega-3 acid ethyl ester content of 55%, the amount of eicosapentaenoic acid ethyl esters and docosahexaenoic acid ethyl esters together is not less than 50% and the content of eicosapentaenoic acid ethyl esters is not less than 40%; for a total omega-3 acid ethyl ester content of 60%, the amount of eicosapentaenoic acid ethyl esters and docosahexaenoic acid ethyl esters together is not less than 50% and the content of docosahexaenoic acid ethyl esters is not less than 40%; and for a total omega-3 acid ethyl ester content of 65%, the amount of eicosapentaenoic acid ethyl esters and docosahexaenoic acid ethyl esters together is not less than 50%, the content of eicosapentaenoic acid ethyl esters is not less than 25%, and the content of docosahexaenoic acid ethyl esters is not less than 20%. Tocopherol may be added as an antoxidant.

A light yellow liquid with a slight fish-like odour. Practically insoluble in water; very soluble in acetone, in dehydrated alcohol, in heptane, and in methyl alcohol. Store in airtight containers under inert gas. Protect from light.

Ph. Eur. 6.2 (Omega-3-Acid Ethyl Esters 90). A mixture of ethyl esters of omega-3 acids. They are obtained by transesterification of the body oil of fat fish species coming from families such as Engraulidae, Carangidae, Clupeidae, Osmeridae, Salmonidae, and Scombridae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (timnodonic acid), heneicosapentaenoic acid, clupanodonic acid, and docosahexaenoic acid (cervonic acid). The total amount of omega-3 acid ethyl esters is not less than 90%, and that of both eicosapentaenoic acid ethyl esters and docosahexaenoic acid ethyl esters together is 80%; the content of eicosapentaenoic acid ethyl esters is not less than 40% and of docosahexaenoic acid ethyl esters is not less than 34%. Tocopherol may be added as an antoxidant.

A light yellow liquid with a slight fish-like odour. Practically insoluble in water; very soluble in acetone, in dehydrated alcohol, in heptane, and in methyl alcohol. Store in airtight containers under inert gas. Protect from light.

Omega-3 Marine Triglycerides

Deniz Kaynaklı Omega-3 Trigliseridler; Poisson (huile de) riche en acides oméga-3 (fish oil, rich in omega-3-acids); Saumon d'élevage, huile de (salmon oil, farmed); Triglicéridos marinos omega 3.

Омега-3 Триглицериды Морского Происхождения

NOTE. Omega-3 Marine Triglycerides (BAN) is a mixture of triglycerides of fatty acids from marine fish containing the equivalent of about 18% of eicosapentaenoic acid and 12% of docosahexaenoic acid. The content of triglycerides is not the same as that in Omega-3-Marine Triglycerides BP.

Pharmacopoeias. *Eur.* (see p.vii) includes Omega-3-Acid Triglycerides, Fish Oil, Rich in Omega-3-Acids, and Salmon Oil, Farmed. *US* includes Fish Oil containing Omega-3 Acids.

Ph. Eur. 6.2 (Omega-3-Acid Triglycerides; Omega-3 Acidorum Triglycerida; Omega-3-Marine Triglycerides). A mixture of mono-, di-, and triesters of omega-3 acids with glycerol, containing mainly triesters. They are obtained by esterification of concentrated and purified omega-3 acids with glycerol or by transesterification of the omega-3 acid ethyl esters with glycerol. The omega-3 acids are from the body oil of fatty fish species coming from families such as Engraulidae, Carangidae, Clupeidae, Osmeridae, Salmonidae, and Scombridae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (timnodonic acid), heneicosapentaenoic acid, clupanodonic acid, and docosahexaenoic acid (cervonic acid). The total amount of omega-3 acids expressed as triglycerides is not less than 60% and that of both eicosapentaenoic acid and docosahexaenoic acid together, expressed as triglycerides, is not less than 45%. Tocopherol may be added as an antoxidant.

A pale yellow liquid. Practically insoluble in water; slightly soluble in dehydrated alcohol; very soluble in acetone and in heptane. Store in well-filled, airtight containers under inert gas. Protect from light.

Ph. Eur. 6.2 (Fish Oil, Rich in Omega-3-Acids; Piscis Oleum Omega-3 Acidis Abundans). The purified, winterised, and deodorised fatty oil obtained from fish of the families Engraulidae, Carangidae, Clupeidae, Osmeridae, Scombridae, and Ammodytidae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (timnodonic acid), heneicosapentaenoic acid, clupanodonic acid, and docosahexaenoic acid (cervonic acid). The minimum content, expressed as triglycerides, is eicosapentaenoic acid 13%, docosahexaenoic acid 9%, and total omega-3 acids 28%. Antoxidants may be added.

A pale yellow liquid. Practically insoluble in water; slightly soluble in dehydrated alcohol; very soluble in acetone and in heptane. Store in well-filled, airtight containers under inert gas. Protect from light.

Ph. Eur. 6.2 (Salmon Oil, Farmed; Salmonis Domestici Oleum). The purified fatty oil obtained from fresh farmed *Salmo salar*. The positional distribution (β(2)-acyl) is 60 to 70% for docosahexaenoic acid (cervonic acid), 25 to 35% for eicosapentaenoic acid (timnodonic acid), and 40 to 55% for moroctic acid. The sum of the contents of eicosapentaenoic acid and docosahexaenoic acid, expressed as triglycerides, is 10.0 to 28.0%. Authorised antoxidants may be added. A pale pink liquid. Practically insoluble in water; slightly soluble in dehydrated alcohol; very soluble in acetone and in heptane. Store in well-filled airtight containers under an inert gas. Protect from light.

USP 31 (Fish Oil containing Omega-3 Acids). The purified, winterised, and deodorised fatty oil obtained from fish of the families Engraulidae, Carangidae, Clupeidae, Osmeridae, Scombroidae, and Ammodytidae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (EPA), heneicosapentaenoic acid, docosapentaenoic acid, and docosahexaenoic acid (DHA). It contains not less than 28% (w/w) of total omega-3 acids (expressed as free acids) consisting of not less than 13% of EPA and not less than 9% of DHA. Antoxidants may be added. A pale yellow liquid. Practically insoluble in water; slightly soluble in anhydrous alcohol; very soluble in acetone and in heptane. Store in airtight containers at a temperature of 20° to 25°, excursions permitted between 15° and 30°. It may be stored under vacuum or under an inert gas. Protect from light.

Adverse Effects and Precautions

The most common adverse effects of omega-3 fatty acid preparations are gastrointestinal disturbances, particularly at high doses, including nausea, eructation, vomiting, abdominal distension, diarrhoea, and constipation. There have been rare reports of acne and eczema. Moderate increases in hepatic transaminases have been reported in patients with hypertriglyceridaemia.

Preparations vary widely in concentration and purity. Some preparations contain significant amounts of vitamins A and D and long-term use could cause toxicity. There is a theoretical possibility of vitamin E deficiency with long-term use, although many preparations contain vitamin E as an antoxidant. Concern has been expressed over the high calorific value and cholesterol content of some preparations.

Omega-3 fatty acids have antithrombotic activity and should be given with caution to patients with haemorrhagic disorders or to those receiving anticoagulants or other drugs affecting coagulation. Hepatic function should be monitored in patients with hepatic impairment, particularly if receiving high doses. Caution may also be required in asthmatic patients sensitive to aspirin since omega-3 fatty acids may affect prostaglandin synthesis (but see Inflammatory and Auto-immune Disorders, below, for studies of fish oils in the management of asthma).

◊ Reviews.

1. Bays HE. Safety considerations with omega-3 fatty acid therapy. *Am J Cardiol* 2007; **99** (suppl): 35C–43C.

Effects on the blood. Omega-3 fatty acids have antithrombotic effects and may increase bleeding. In a study[1] in adolescents with familial hypercholesterolaemia, epistaxis occurred in 8 of 11 patients treated with a fish oil supplement; prolonged bleeding time was noted in 3 patients. There have also been case reports of INR elevation and haematoma in patients taking fish oil preparations with antithrombotics (see Lipid Regulating Drugs under Interactions of Warfarin, p.1431), although controlled studies have failed to show an effect.

1. Clarke JTR, *et al*. Increased incidence of epistaxis in adolescents with familial hypercholesterolemia treated with fish oil. *J Pediatr* 1990; **116:** 139–41.

Effects on glucose metabolism. Although a deterioration in glycaemic control has been reported in diabetic patients taking omega-3 fatty acids and fish oil preparations, a meta-analysis[1] of studies in type 1 and type 2 diabetics, and a systematic review[2]